Again, in both cases the symptoms of diabetes were decidedly more aggravated in the second pregnancy, and in case No. 1 a severe diabetes developed which persisted after pregnancy terminated.

Using the analogy of Dr. Allen previously quoted, that a diabetes is a sign of a weak pancreas just as distress and indigestion after eating signifies a weak stomach, it seems reasonable to assume that in the second pregnancy the pancreas was much weaker than in the first. It also suggests that in some way pregnancy threw an extra burden on the pancreas.

The most recent addition to the literature on this subject is a series of fourteen cases reported and discussed by Joslin.[4] None of these cases, however, were recent enough in order that the Allen treatment might have been tried. Fasting was tried in one case in the series, resulting in a decrease in sugar. Quoting Joslin on this case, he says, "Pregnancy occurred for a third time in April, 1905, but this time the quantity of sugar was not as easily controlled as before. It is interesting that the patient was fasted one week by Dr. Taylor in his efforts to lower the sugar, and as a matter of fact it did decrease to 2.1%. But in August it was 6.7%. In October, 1905, the six month of pregnancy, 5.8% of sugar was present."

In analyzing these fourteen cases I find:

Two died in coma; one committed suicide on becoming pregnant the second time; two are still alive but with diabetes; one had diabetes much worse in the third pregnancy, tuberculosis set in one month before her death, and sugar disappeared from her urine the day before her death; three had one pregnancy, are now alive and well; three had three pregnancies, sugar in each pregnancy, now alive and well; one had two pregnancies, sugar in each pregnancy, now alive and well; one had two pregnancies, sugar beginning in the eighth month in the first pregnancy, and in the second month in the second pregnancy.

Of the four cases that died, three of the number had diabetes before pregnancy occurred, while eleven cases developed diabetes during pregnancy.

Taking the sixteen cases reported in this paper, only fifty per cent. were free from diabetes at the time of the reports, and of these, nineteen per cent. had only one pregnancy. Fifty per cent. either have died or still have diabetes. Eighty-one per cent. developed diabetes during pregnancy.

Conclusions.

1. If sugar, even in the slightest amount, appears in the urine during pregnancy, the Allen treatment should be begun at once, since this method of treatment has met with the most favorable results in uncomplicated diabetes.

2. If the sugar does not disappear under this treatment, pregnancy should be terminated.

3. Whether pregnancy sets up a latent diabetes is as yet not proved. In many cases, however, where diabetes has developed in pregnancy, a succeeding pregnancy causes an earlier and more aggravated recurrence of the diabetes, which, in some cases, persists after the termination of pregnancy.

4. Pregnancy occurring in a diabetic offers a more grave prognosis than diabetes occurring in pregnancy.

5. Unless a carbo-hydrate equilibrium can be absolutely maintained in a diabetic woman, she should be advised to avoid pregnancy.

Bibliography.

1. Edgar, Prin. and Practice of Obstetrics, p. 344.
2. Allen, Treatment of Diabetes. Boston Med. and Surg. Jour., Feb. 18, 1915, p. 243.
3. Ibid.
4. Joslin, Diabetes in Pregnancy. Boston Med. and Surg. Jour., December 2, 1915, p. 841.

USE OF WHOLE BLOOD IN HEMORRHAGE.*

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It was the original intention to deal only with the intramuscular injection of whole blood in the treatment of hemorrhage. But on reviewing the literature on this subject, I found it necessary to wander into the different hemorrhagic diseases and consider their causes and some of the different methods of treatment of these conditions by sera.

At present we are unable to make a classification, as we do not know the causes of the so-called hemorrhagic diathesis. Moss catalogues the most common diseases with which hemorrhage is or may be associated:

Hemophilia (hereditary and spontaneous).

Hemorrhagic Disease of New Born (several forms).

The Purpuras, acute and chronic (simple, rheumatic, and senile).

Jaundice.

Grave Anaemias and severe infections.

It is generally considered that the coagulation of blood depends upon the action of a fibrin ferment (which is normally formed only after the blood is shed) on the fibrinogen which is in the circulating blood. Concerning its formation, the use to which it is put in the body or its fate, we know little. The fibrin ferment-complex is now usually designated as "thrombin," a term given it by A. Schmidt. Thrombin has been isolated and studied by Howell and others. Howell showed that when thrombin was added to a solution of fibrinogen, that coagulation took place by the formation of fibrin. So it was shown that the substances, fibrinogen and thrombin, together form the essential feature of blood clot. Their mode of action is not known, whether it is a chemical, psycho-chemical, or a ferment. Thrombin only occurs in shed blood. It does not extend to the circulating blood. Hence it seems evident that all the elements which enter into its formation must be present before it is shed. To this the name "prothrombin" or "thrombogen" has been given.

To account for the conversion of prothrombin into thrombin, the presence of a ferment is assumed, which has been called by Morawitz "thrombokinase." It has been found that the presence of calcium is essential to the action of thrombokinase.

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In converting prothrombin into thrombin the exact role played by the calcium salts remains unsettled.

What is the origin of the kinase? There are several theories. It is known that as soon as the blood is shed there is a disintegration of the blood platelets and also of the leucocytes.

Duke in his article on the "Relation of Plates to Hemorrhagic Disease" points out that there is a marked diminution of blood plates in these hemorrhagic conditions, and that when these are supplied by transfusion the bleeding stops for a time, but with a reduction of these elements again hemorrhage will occur. The blood plates have been demonstrated to be the nuclei about which is concerned the formation of fibrin. However, in some cases the coagulation time is normal, but it is generally prolonged, and sometimes decomposition takes place without clot. W. H. Howell (Am. Journ. Phys., xxvii, p. 453, and xix, p. 187) demonstrates that the retardation or suppression of clotting is frequently attributable to the action of an antithrombin which neutralizes thrombin and that only after removal of the antithrombin or the addition of a further amount of thrombin can coagulation be induced. It is also possible especially in cases of cirrhosis that the fibrinogen content of the blood may fall, so that even in the presence of an adequate proportion of thrombin, the clot found is not sufficient (Whipple).

It would seem that in the majority of cases of pathological hemorrhages, thrombin is not liberated in sufficient quantity or rapidly enough to produce the desired clot. Other theories, such as an abnormal thinness of vessel walls, abnormal high blood pressure, a disproportion between the total amount of blood and the total capacity of the vascular system have been advanced; and in hemophilia an obscure explanation as to inherited chemical (fermentation) degeneration of the protoplasm of the formed elements of the blood or the whole organism (Morawitz and Losen), or again the lack of one or more factors normally present, that are concerned in the process of coagulation: as, the lack of fibrinogen, calcium salts, prothrombin, or thrombikinase.

Welch (Trans. College of Phys., Vol. xxxii, 1912, p. 382) believes the underlying condition in these bleeding cases has to do with the endothelial lining of vessels, etc.; that there is a disturbance of balance of the ferments of the cells, due to malnutrition, evidenced by hemorrhage into serous cavities. In bleeding babes he observes there is a marked putrefaction, hypersecretion of mucus, and decomposition in the intestinal tract accompanied by the formation of toxins, which are absorbed and interfere with nutrition of the endothelium, possibly causing cloudy swelling, and thereby upset the normal balance normally attained between the ferments and antiferments of these cells. The toxins or this various condition are equally capable of destroying this equilibrium.

When normal serum from whatever source is added to the blood of any of these cases, it will cause prompt clotting. From this it is reasoned that there is lacking in the blood of some otherwise normal individuals a kinase or activating substance that would normally cause coagulation. It is argued, however, that it is not for this reason that the hemorrhage stops, but for quick nutritional repair of the damage done the endothelial lining of vessels, by action of toxins of bacteria, intestinal, septicemic, etc.

The disease "melena neonatorum"† in many and perhaps all instances is characterized by a relatively sudden disappearance of prothrombin from the blood; the condition usually develops during the first two weeks after birth, and is often fatal; possibly due to lack of formation in the liver of prothrombin.

Bernwald was one of the first to treat a case of hemophilia with serum in 1897. In 1902 Welch reported good results in the treatment of melena neonatorum by the use of normal human serum, probably as much as 300 c.c. He also used small doses over a long period, nine months, as much as 3500 c.c.m., using it for the nutritional value.

Almost every form of serum has been used and from all good results have been reported. Among the sera used are rabbit, horse, antitoxic sera, normal human, citrated blood, pipetted blood, and whole blood (human). The injection of the serum of animals, on account of the difference of species, by reason of the metameric protoid content, is capable of sensitizing (as with other foreign protoids) with the cardinal symptoms of anaphylaxis (serum sickness); the homologous sera do not, and rather tend to be of distinct nutritative value, especially in the malnutrition of infants, who cannot take nourishment by mouth (Welch).

In 1908 Schloss and Cominsky reported good results with use of normal human serum and whole blood subcutaneously in hemorrhage of the new born. Curtis used whole blood in uterine hemorrhage with success and suggests that it should be used with benefit in the anemias, wasting disease infections, and might even prove better than transfusion. It would seem from the foregoing that the method which will supply or stimulate the elements concerned in the clot formation is the one of choice. Transfusion would come first, but it is so surrounded by technical difficulties, difficulty in obtaining a suitable donor; as the blood to be of use and without danger to the patient, must be taken from the group (according to isoagglutinant reaction) to which the patient belongs (Moss), thus avoiding the danger from isoagglutination and isomerolysis. The time delay makes it ineffective. Defibrinated blood and thrombin citrated blood have the same objection. A report of a successful case of purpura treated by H. Wohltram is given in Journal Amer. Med. Assoc., 2163, Dec. 18, '15 (70 c.c. of 2% sodium citrate in 85% Na cl to 100 c.c. of blood and inject).

Normal serum takes time to separate from the whole blood and soon becomes inactive by the formation of metathrombin. H. A. Clowes and F. C. Bush, Int. Med. June 14, 1913, p. 16, advocate acetone pipetted blood. The technical difficulties here again occur. Fresh rabbit's serum seems to

† Whipple. Arch. Int. Med., 1913, p. 636.

be the best of the animal sera, but must be used fresh, as thrombin soon changes into metathrombin on standing for any length of time. It is less toxic than horse serum and does not sensitize so quickly.

It has been demonstrated that the simplest, quickest, and most efficient method is to obtain about 20 c.c.m. of blood from the vein of a healthy person and inject immediately into the gluteal muscles of the patient. Two needles should be used—one can be inserted into the patient, so as to save time. These intramuscular injections are not painful nor do they leave any bad results, but are promptly absorbed. It seems strange that with the results obtained that there have been so few reports; probably on account of the simplicity of the method. I wish here to report six cases, three of which I treated and three in the service of Dr. A. B. Spalding. I will cite Dr. Mohun's case first.

In February, 1915, I saw a baby (in consultation with Dr. C. C. Mohun) with melena neonatorum. It was a high forceps case, delivery not especially difficult. On the fifth day there was a tarry stool; these increased to six to eight a day for sixth, seventh, and eighth day. On the ninth day I saw the patient and suggested the injection of whole human blood into the muscles of the buttock. This I did, taking 10 c.c.m. from the father. On the tenth day there were three tarry stools. After this there were no more and a complete recovery followed.

L. L., age 3, also seen with Dr. Mohun on February 15, '15. The first symptom was the passing of bloody urine. There was no increase of temperature, pulse 90. No pain or frequent urination. Physical examination revealed no cause for the bloody urine. Calcium lactate failed after three weeks of medical treatment. At this time I saw her and gave 10 c.c.m. of the mother's blood. The bleeding ceased almost immediately and she had no further trouble and has had no recurrence of the trouble since.

The next case was a remarkable one from the standpoint of the use of the whole blood, or it was a remarkable coincidence.

Baby C., age 2½. A fine, large girl, always normal, healthy, and happy. Fell from off a chair, striking her side over the right kidney region. She did not complain at the time. But in about three weeks she commenced to pass bloody urine. She had no pain, rise of temperature, or other apparent disturbance. She was given the usual medical treatment for three weeks without the desired results. I saw her at this time. Physical examination did not reveal anything. Wassermann negative. Examination of the urine shows diffuse mixture of red cells; no clots; x-ray negative. She was not anemic. It was decided to try the whole human blood and I gave her 10 c.c.m. of the father's blood into the gluteal muscles. That night the urine showed small clots of blood; then there was a complete cessation of the blood except microscopical cells. We were elated over the result. But the blood again showed on the sixth day after the injection. She was then given an anaesthetic and an examination through the rectum and palpation revealed a tumor mass of the kidney. The following day the kidney was removed by Dr. Barbat, and showed a large sarcoma of the endothelial type, occupying the middle part, leaving both poles free. It was the size of a hen's egg. It extended in a pyramid from the apex at the pelvis of the kidney. The point of this showed blood clot and was the point of the bleeding. We cannot say that the injection caused the clot formation, but it seems that perhaps it did, and that on the fifth or sixth day the clot loosened and the hemorrhage was renewed. The child recovered nicely and has been well since. This was about two months ago.

The next three cases were taken from the clinical records of the obsterrical department through the kindness of Dr. A. B. Spalding:

Baby R. Born February 26, '15. Spontaneous delivery. February 28 passed blood; kept quiet and not nursed. 30 c.c. of mother's blood was allowed to stand and the serum to separate out; then injected subcutaneously. March 1 vomited small amount of blood and 15 c.c.m. of mother's blood serum was injected under skin between shoulders. March 2, stool dark red blood; 5 c.c.m. of whole blood from the father injected into gluteal muscle. March 3, no further hemorrhage. March 10, in good condition, discharged, cured.

Baby L., born March 12, '15. Low forceps. Stool showed high intestinal hemorrhage, tarry. March 27, calcium lactate x.x. Was given 5 c.c. of maternal blood intravenously and 10 c.c. into buttocks, still some blood, but much less jaundiced, but improved. At 5:30 same hemorrhage, given 10 c.c. intramuscularly. June 1, 5 c.c.m. into the muscle. June 3, jaundice gone; gaining weight. June 24, discharged, O. K.

Baby girl, born May 27, '15, spontaneous. May 27: Regurgitating small amount of dark material resembling digested blood. Blood in stools (bladder suspected). Has marked haematoma on right side of head. Given 9 c.c. of mother's blood, intramuscularly. June 1, no further symptoms. June 2, O. K. June 7, O. K. June 8, discharged in perfect condition.

Mr. M., age 36. Had a severe hemorrhage from the bowels. Haemoglobin 50%. Reds 2,500,000. Was given horse serum every three days for four times, also calcium lactate was given regularly. The stools were tarry, the hemoglobin still decreased to 30%, reds 1,500,000. He was then given 20 c.c.m. of whole human blood into the gluteal muscles. The stools cleared immediately and all hemorrhage ceased. He rapidly gained his hemoglobin and red cells and at the end of two weeks his hemoglobin was 90%, reds 4,500,000. Diagnosis: Probable duodenal ulcer.

THE ATTITUDE OF THE PHYSICIAN TOWARD THE VENEREAL PATIENT.*

By ALBERT M. MEADS, M. D., Oakland.

Those of you who have read in the American Magazine of last April, Richard Cabot's article entitled "Better Medicine at Less Cost," will get a great deal of entertainment in looking over the remarks that that paper stimulated those on the other side to pass through the medium of the Medical Press. One letter in particular, published in the Boston Medical Journal for May, will be well worth while reviewing, especially if you enjoy seeing Greek meet Greek.

This author, who has the audacity to reprimand one of his fellow Bostonians, especially Dr. Cabot, has conducted his argument in such a masterly manner that the reader, whether friend or foe to socialized medicine, cannot help but be convinced that there are two sides to the question. Moreover, the faults of the modern dispensary system

* Read before the Alameda County Medical Society September 19, 1916.